



### AMENDMENTS TO THE CLAIMS

1. (Previously presented) A method of identifying a compound that is an allosteric modulator of intermolecular interactions from a distal site at a functionally critical site between a target protein and a modifier, which method comprises the steps of

a) identifying an allosteric cavity on a target protein that is a measurable distance from the functionally critical site of said target protein, said cavity being a candidate site for interacting with an allosteric modulator;

b) calculating the dimensions of said cavity and mapping the chemical and/or electrostatic properties of said cavity;

c) identifying compounds that contain functional groups that can be accommodated by said cavity;

d) testing said compounds in an in vitro assay to detect a compound which binds within the cavity of said target protein and allosterically modulates intermolecular interactions at the functionally critical site between said target protein and said modifier;

thereby identifying a compound that is an allosteric modulator of interactions at the functionally critical site between said target protein and a modifier.

2. (Withdrawn) A pharmaceutical composition comprising:

a) a pharmaceutically acceptable carrier of diluent; and

b) a therapeutically effective amount of a compound having a structure selected from the group consisting of Formulae I-XIX.

3. (Withdrawn) A method of treating an individual suffering from an inflammatory condition comprising the step of administering to said individual a therapeutically effective amount of a compound having a structure selected from the group consisting of Formulae I-III.

4. (Withdrawn) A method of treating an individual suffering from an undesirable immune response or immunological condition comprising the step of administering to said individual a

therapeutically effective amount of a compound having a structure selected from the group consisting of Formulae I-VI.

5. (Withdrawn) A method of treating an individual suffering from a bacterial infection comprising the step of administering to said individual

- a) penicillin or a penicillin derivative antibiotic; and
- b) a compound having a formula selected from the group consisting of Formulae VII-XIX.

6. (Previously presented) The method of claim 1, wherein step (c) comprises detecting shape complementarity between the functional group of the compound and the cavity.

7. (Previously Presented) The method of claim 1, wherein step (d) comprises detecting a compound that inhibits intermolecular interactions between said target protein and said modifier.

8. (Previously presented) The method of claim 1, wherein step (d) comprises detecting a compound that enhances intermolecular interactions between said target protein and said modifier.

9. (Withdrawn) The method of claim 1, wherein the target protein is selected from the group consisting of a membrane-bound protein, a cytosolic protein, a nuclear protein, an enzyme, a cytokine, a lymphokine, a chemokine, an adhesion molecule, a growth factor, and a receptor thereof.

10. (Withdrawn) The method of claim 9, wherein the target protein is a receptor.

11. (Withdrawn) The method of claim 9, wherein the receptor is a member of the TNF receptor superfamily.

12. (Withdrawn) The method of claim 11, wherein the TNF receptor superfamily member is selected from the group consisting of the TNF receptor, fas, CD40, gp120, fas ligand, TNF- $\alpha$ ,

$\beta$ -lactamase, c-erbB2, growth hormone receptor, growth hormone, insulin receptor, insulin, IL-1 receptor, IL-1, IL-2 receptor, IL-2, epidermal growth factor receptor (EGFR), and epidermal growth factor.

13. (Withdrawn) The method of claim 12, wherein the TNF receptor superfamily member is a TNF receptor.

14. (Withdrawn) The method of claim 9, wherein the target protein is an enzyme.

15. (Withdrawn) The method of claim 14, wherein the enzyme is  $\beta$ -lactamase.

16. (Withdrawn) The method of claim 9, wherein the target protein is a member of the immunoglobulin superfamily.

17. (Withdrawn) The method of claim 16, wherein the target protein is CD4.

18. (Withdrawn) The method of claim 1 wherein the modifier is a protein, a non-proteinaceous molecule, or a non-organic molecule.

19. (Withdrawn) The method of claim 18, wherein the modifier is a protein selected from the group consisting of a membrane-bound protein, a cytosolic protein, a nuclear protein, an enzyme substrate, a cytokine, a lymphokine, a chemokine, an adhesion molecule, a growth factor, or a receptor thereof.

20. (Withdrawn) The method of claim 18, wherein the modifier is a member of the TNF receptor superfamily.

21. (Withdrawn) The method of claim 18, wherein the modifier is selected from the group consisting of TNF receptor, fas, CD40, gp120, fas ligand, TNF- $\alpha$ ,  $\beta$ -lactam, c-erbB2, growth hormone receptor, growth hormone, insulin receptor, insulin, IL-1 receptor, IL-1, IL-2 receptor, IL-2, epidermal growth factor receptor (EGFR), MHC/antigen/TCR complex, and epidermal growth factor.

22. (Withdrawn) The method of claim 21, wherein the modifier is TNF- $\alpha$ .

23. (Withdrawn) The method of claim 19, wherein the modifier is  $\beta$ -lactam.

24. (Withdrawn) The method of claim 19, wherein the modifier is the MHC/antigen/TCR complex.

25. (Currently amended) The method of claim 1, wherein identifying the allosteric cavity within the structure of a target protein in step b) a) comprises identifying thermal  $\beta$  factors, using calorimetric values from thermodynamic studies, or using computer simulation algorithms using nuclear magnetic resonance, crystal structure analysis, calorimetric values from thermodynamic studies, or computer modeling.

26. (Previously presented) A method of identifying a compound that is an allosteric modulator of an intermolecular interaction associated with a biological function intended to be modulated at a functionally critical site between a target protein and a modifier, which comprises:

a) identifying an allosteric cavity on a target protein that is a measurable distance from the functionally critical site on the target protein, said cavity being a candidate site for interacting with an allosteric modulator;

b) calculating the dimensions of said cavity and mapping the chemical and/or electrostatic properties of said cavity;

c) identifying compounds that contain functional groups that can be accommodated by said cavity;

d) testing said compounds in an in vitro assay to detect a compound which modulates the interaction at the functionally critical site between the target protein and the modifier.

27. (Currently amended) A method of identifying a compound that is an allosteric modulator of an intermolecular interaction at a functionally critical site on a target protein, the intermolecular interaction at the functionally critical site occurring between the target protein and a modifier, and being associated with a biological function to be modulated, which method comprises:

a) identifying an allosteric cavity on a target protein that is a measurable distance from the functionally critical site on the target protein, said cavity being a candidate site for binding an allosteric modulator;

b) calculating the dimensions of said cavity and mapping the chemical and/or electrostatic properties of said cavity;

c) identifying compounds that contain functional groups that can be accommodated by said cavity;

d) testing said compounds in an in vitro assay to detect a compound which modulates the interaction at the functionally critical site between said target protein and said modifier.

28. (Previously presented) A method of identifying a compound that is an allosteric modulator of an intermolecular interaction associated with a predetermined biological function to be modulated, said interaction occurring between a target protein and a modifier at a functionally critical site on a target protein, which method comprises:

a) identifying an allosteric cavity that is a measurable distance on the target protein

from the functionally critical, said cavity being a candidate site for accommodating an allosteric modulator;

- b) calculating the dimensions of said cavity;
- c) mapping the chemical and/or electrostatic properties of said cavity;
- d) identifying compounds that contain functional groups that can be accommodated by said cavity;
- e) testing said compounds in an in vitro assay to detect a compound which modulates the interaction at the functionally critical site between said target protein and said modifier;

thereby identifying a compound that is an allosteric modulator of the interaction at the functionally critical site between said target protein and a modifier.

29. (Currently amended) A method of identifying a compound that is an allosteric modulator of an intermolecular interaction at a functionally critical site on a target protein, wherein the intermolecular interaction at the functionally critical site is between the target protein and a modifier, and wherein the interaction is associated with a predetermined biological function to be modulated, which method comprises:

- a) identifying an allosteric cavity on a target protein that is a measurable distance from the functionally critical site on the target protein, said cavity being a candidate site for accommodating an allosteric modulator;
- b) calculating the dimensions of said cavity and mapping the chemical and/or electrostatic properties of said cavity;
- c) identifying compounds that contain functional groups that can be accommodated by said cavity;
- d) testing said compounds in an in vitro assay to detect a compound which modulates the interaction at the functionally critical site between said target protein and said modifier;

thereby identifying a compound that is an allosteric modulator of the interaction at the functionally critical site between said target protein and a modifier.

30. (Previously presented) A method of identifying a compound that is an allosteric modulator of an intermolecular interaction at a functionally critical site, wherein the functionally critical site is the site of the intermolecular interaction between a target protein and a modifier that is necessary for the specific biological function attributed to the target protein, which method comprises the steps of

a) identifying an allosteric cavity on a target protein that is a measurable distance from the functionally critical site on the target protein, said cavity being a candidate site for binding an allosteric modulator;

b) calculating the dimensions of said cavity and mapping the chemical and/or electrostatic properties of said cavity;

c) identifying compounds that contain functional groups that can be accommodated by said cavity;

d) testing said compounds in an in vitro assay to detect a compound which modulates the interaction at the functionally critical site between said target protein and said modifier;

thereby identifying a compound that is an allosteric modulator of the interaction at the functionally critical site between said target protein and a modifier.

31. (New) The method of claim 25, wherein the allosteric cavity is identified using nuclear magnetic resonance or crystal structure analysis, and further comprises identifying thermal  $\beta$ -factors.